

cicatricial stenosis been observed in the animals which were allowed to live from 44 to 100 days. In closing, it may be emphasized that in the endeavor to reduce to a minimum the percentage of mortality in this palliative operation, the aim is to replace by the gastroenterostomy in the most cases, as much as possible, the dangerous and not radical pylorotomy.

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THE PRESENT STATE OF KNOWLEDGE AS TO CARCINOMA.

CARCINOMA is the most frequent tumor found in the human body, as well as the most fatal. The points to be considered, from the standpoint of the practical surgeon, in connection with the subject, relate mainly to the cause of the disease, its prognosis and treatment.

The question of the origin of carcinoma through the medium of a specific micro-organism is one of great interest and practical importance. More than a century ago the question was raised of the transferability of the disease. In the light of now well-demonstrated facts concerning the origin of tuberculosis, syphilis and leprosy, the subject of the analogy existing in this respect between these diseases and carcinoma has been vigorously agitated. The resemblances between the first named and the disease under discussion are striking. In both, a strictly local origin of the tumor is observed, occurring in almost every part of the body. Then a preference to some extent for certain regions is observed in both, as well as the occurrence of secondary growths in distant parts through the medium of the lymph channels and lymphatic glands. It is not to be supposed that this can occur from the propagation of the secretions of the tumor or the so-called cancer juice, or from any chemical poison. It is improbable that this could possess the power of infecting alike tissues of such widely-varying characteristics, and in such distant parts. Skin and glands, connective tissue and bone, all show, when attacked, the same peculiar cell structure found in the primary focus.

Histological studies have demonstrated the fact that not only the liquid but the cellular portions of the tumor find their way into the lymph channels and lodge in the lymphatic glands, in which latter situation secondary nodules develop, this being followed, in its turn, by breaking down of the glands, and the direct passage thereafter of the infectious agents into the general circulation.

While it is not difficult to understand the method of transference of these cellular elements from one portion of the body to another, the question still remains, How do these obtain the power of proliferating or of establishing a new colony, the atypical growth of which either forces the surrounding tissues to take part or suffer destruction? It may be said in reply to this, that normal epithelial structures, when transplanted, immediately take on growth, as shown in certain plastic operations, and that transplantation of muscle, nerve and bone is now an accomplished fact. This is true, but these never exceed the normal limits of growth; tumor is never produced as a result of such transplantation. If a proliferation occurs in excess of the requirements of repair, as, for instance, the formation of callus after bone transplantation, this is quickly absorbed. It is, therefore, reasonable to suppose that a specific infectious agent exists in carcinoma, and that this is disseminated, accompanied or otherwise, by the cellular elements of the original neoplasm, through the lymph channels or blood-vessels. The identification of these with micro-organisms in the near future is highly probable, as well as the demonstration of the manner in which these infect the cells. It may be said, in passing, that Virchow held that the influence which affected the cells was similar to the action of the spermatozoa upon the ovum.

The attempt to prove that such specific agents existed by demonstrating the contagiousness of malignant growths has always given but indifferent results, and the data derived from these experiments are therefore unreliable. The experiments of von Langenbeck are well known. The injection of fluid from a recently removed cancerous growth into the circulation of a dog was followed by the occurrence of a carcinomatous nodule in the lung of the animal. A number of

experimenters followed this attempt, some of whom obtained positive, while in others only negative results followed. One fact, however, is noticeable: while those who employed material obtained directly from the patient, or from a recently removed growth, and at the same time secured primary union in the inoculation wound, succeeded the most frequently, on the other hand, those who employed material taken from the dead body, or in whose hands the inoculation wound suppurated, recorded the largest relative number of failures.

In addition to these experimental studies, clinical observation at least suggests the possibility of the disease being transported from one person to another. Munde, Macewen, Parry and others, during the past decade have communicated cases which seemed to prove that an attendant could be infected with the disease, and that the husband could be infected upon the penis from uterine cancer in the wife.

The subject of the contagiousness of carcinoma is receiving a more than usual amount of attention at the present time. Guelliot, a French observer, has made a most careful study of the entire question during the past year and brings forward some extraordinary facts which seem, upon examination, to point to the great probability of the contagious nature of the disease.¹

As to the predisposing causes: At the present time it is believed that these, save those referable to age and local conditions, have very slight influence in the production of the disease. The causes assigned by the older writers, namely, malnutrition, grief, heredity, etc., are now scarcely considered of sufficient importance to enter into the question at all; in point of fact, the experience of competent observers suggests that the first-named condition rather favors resistance to the disease, both in its onset and subsequent course.

It is a well-known fact that epithelial carcinoma selects, by preference, the natural outlets of the body, and particularly narrowed portions of canals lined with mucous membrane. It is a question worthy of consideration whether this is not due to the fact that these points are more exposed to injury, and furnish ready means of access

¹ Samuel Lloyd, in *ANNALS OF SURGERY*, February, 1893.

for specific irritating or infectious agents. And may it not likewise be true that the occurrence of carcinoma at the site of lupus and leg ulcers may be accounted for in the same manner?

Predisposition, based upon chronic influences, is to be assigned a place in the consideration of the etiology of carcinoma. Its frequent occurrence upon the scrotum in chimney-sweeps, paraffin-workers, and others on whom soot accumulates, and in whom a chronic eczema precedes the development of the disease, is well known. The epithelioma of the smoker's lip is another familiar illustration of the influence of chronic irritation.

Physiological activity has been considered as one of the predisposing causes of carcinoma, particularly in the disease as it attacks the mamma (Sprengel, of Dresden). It may be suggested that excessive lactation only leads to greater frequency of the disease, because of the greater opportunity afforded for the entrance of specific infection through the fissured nipples, to which nursing women are subject.

The persistence of embryonal conditions has long been recognized as the origin of certain tumors of undoubted congenital character, such as capillary angioma and dermoid cysts. Cohnheim undertook to establish a generalization of tumor pathology which should account for malignant diseases, and particularly carcinoma, upon the basis of a foetal origin of the atypical proliferative process. Even should this view ultimately prevail, it still leaves unanswered the question as to what influences are brought to bear by means of which the development of embryonal tissue is accomplished after remaining latent for years.

In the further consideration of the probability of some specific influence, acting as the immediate cause of the disease under discussion, may be mentioned the fact that during the first decade of life the congenital type of tumor is almost exclusively observed; during the second decade, those based upon an atypical proliferation of connective tissue elements (sarcoma), particularly those which attack the medullary structure of bone and the periosteum are the most prominent. These latter may continue to appear in the third as well

as the fourth, but during the fourth and fifth decades of life these growths attack principally the soft parts, rather than the osseous structures (sarcoma of the mamma, testicle, muscles of the thigh, etc.). On the other hand, carcinoma is comparatively rare in the first three decades, although exceptionally it may occur within the third. It therefore must be apparent at a glance that, if both of these classes of neoplasms depend for their origin upon the undue development of embryonal tissue, there must exist some specific influence in the case of each, which leads to a connective tissue proliferation at the expense of the epithelial structures, and occurring at an early period of life on the one hand, or an atypical epithelial proliferation at the expense of the connective tissue elements occurring later in life, on the other. Thiersch's ingeniously devised theory of the battle of the cells cannot meet the requirements.

The importance attributed by the laity, as well as the profession, to heredity is probably very much exaggerated, if, in point of fact, it possesses any influence whatever. Here, as in tuberculosis, an inherited constitutional weakness or want of resistance on the part of the tissues may enter into the consideration, but the existence of a hereditary specific predisposition is not only much doubted, but positively denied. Even if this be granted, as well as the theory of Cohnheim, that this may consist of a collection of epithelial or connective tissue elements in an imperfectly developed foetal state, yet we are as far as ever from any knowledge as to what especially irritating influences govern their proliferation.

Further, the question of so-called malignant metamorphosis has a bearing upon the matter in hand. It is admitted that, under certain circumstances, the growth arising from connective tissue elements, originally of a benign character, may after extirpation recur, and in a form which leaves no doubt that they are the result of atypical development, and hence malignant. In this manner a fibro-sarcoma may follow a simple fibroma, or sarcoma develop from an enchondroma. But such a thing as the metamorphosis of a connective-tissue type of tumor into one of the epithelial type is unknown. The

probable existence of a specific irritant, and that probably a micro-organism, explains, more completely than any other theory, this supposed malignant metamorphosis.

Another circumstance bearing out the analogy of carcinoma to tuberculosis is the tendency of the former, like the latter, to involve neighboring structures, as well as the facility with which the disease is transferred from its original focus to lymphatic glands through the lymph channels. In all probability this infection occurs through the medium of the carcinoma cells, which possess, according to Waldeyer, peculiar contractile as well as migrating properties, and in this manner secondary foci are produced. A peculiar preference is shown by carcinoma for propagation through the lymphatic system. Local growth occurs by infection and invasion of the immediately adjacent lymph channels. This analogous method of dissemination still further suggests the probability that carcinoma, like tuberculosis, is the result of the action of a specific micro-organism.

Propagation by auto-inoculation has likewise been observed. Instances of infection from one vocal cord to that of the opposite side are recorded, as well as carcinoma of the cheek at a point opposite to a similar growth upon the tongue. Contact infection is likewise observed in those cases in which the parietal peritonæum becomes involved secondarily to carcinoma of the liver, or in which the latter occurs following carcinoma of the adjacent transverse colon. The extensive dissemination sometimes observed in the peritoneal cavity, as secondary to a primary focus in a loop of intestine, and which, by constant changes of position of the bowel is brought in contact with new points, can only be explained in this manner.

The theory of a specific micro-organism, although not yet fully confirmed, is the only one at all approaching probability. Rappani, and later Scheurlen, believed that they had discovered a specific microbe, but other observers have failed to confirm this. Recent researches, however, seem to have shown the presence of certain micro-organisms in carcinomatous growths belonging to the class of sporozoa or coccidia. These consist of low protistan organisms, which are

rather frequently found parasitic in man and other vertebrate animals, in which they occupy the skin and intestinal tract. The muscles and blood may likewise contain them, and in two diseases, at least, they are present, namely, *molluscum contagiosum* and that form of papillary dermatitis which occasionally precedes the development of carcinoma of the mamma (Paget's disease of the areola). These protozoa-like parasites, in their relation to carcinoma were first described by Pfeiffer, of Jena, in 1888, who demonstrated their presence in the cells of recently removed melanotic carcinoma. He likewise suggested that different parasites exist in different varieties of carcinoma. The fact of their presence has recently claimed to have been demonstrated by Podwyssozki and Sawtschenko, as well as by Plimmer and Jackson Clarke. The former observers claimed that they had discovered certain falciform bodies which represented stages in the development of the carcinoma parasite. Ohlmacher, at the last meeting of the Pathological Section of the Chicago Academy of Sciences, in pointing out the liability to form wrong conclusions from the appearances produced by the use of some of the rapidly multiplying new micro-technical procedures, particularly those involving the use of safranin and iodine and safranin and picric acid alcohol, calls attention to the studies of Podwyssozki and Sawtschenko, and claims that the falciform and other bodies described by these observers are artificial products due to the use of safranin and iodine or safranin and picric acid in the staining process. Whether or not these sporozoa are the essential specific infecting agents of carcinoma remains to be demonstrated. They may only occur in the course of cell formation or degeneration, and hold but a casual relation to the disease. Their position as etiological factors may possibly be determined by the results of inoculation experiments upon lower animals with pure cultures of the micro-organisms obtained from pure carcinoma, although, according to Jackson Clarke, the sporozoa of carcinoma are more closely related to the hæmatozoa than to the coccidia. Since one stage of their existence is passed in the interior of the cell of another animal, it will not be easy to make artificial cultures of them.

Some very suggestive observations have been made bearing upon this subject by Metschnikoff. He describes a disease occurring in rabbits known as coccidiosis, which is characterized by the presence of coccidia or sporozoa. It consists of nodules found in the liver of the animals, the peculiar and essential characteristic pathological feature of which is an atypical proliferation of epithelial cells, quite analogous to that found in carcinoma in man. This, taken in connection with the demonstrated presence of coccidia in carcinoma, and the fact that the number of the parasites, as found in the latter disease, bears some relation to the malignancy of the type, they being more abundant in medullary growths and but sparingly present in those less disposed to recurrence, and hence less malignant, such as epithelial carcinoma of the face, presents, to say the least, food for reflection, and an incentive to further investigation. The isolation of the specific micro-organism of carcinoma, as well as of sarcoma, and a study of the entire question from the standpoint of the bacteriologist, hold out a far greater hope, at the present time, than any other method of investigation.

There are some interesting and important points relating to the prognosis of carcinoma which might be profitably dwelt upon, but which can only be alluded to briefly here. That the disease is a most distressing one from every standpoint is true beyond a doubt. The prognosis is exceedingly unfavorable for three reasons: (1) Because of the local destruction of tissue; (2) because of the final invasion of the entire organism; (3) for the reason that, even when apparently radically extirpated, recurrence is the rule, and not the exception.

The proportion of cases in which recurrence takes place will vary with the character of the growth, its accessibility to radical operative interference, and the period of the disease which has been reached prior to the operation. The kind of recurrence, whether regionary or dyscrasial, will also be governed, to some extent, by these considerations. In carcinoma of the lip and of the mamma, for instance, owing to the accessibility of the growth, as well as its lymphatic sequelæ, its ready recognition and hence more frequent early and radical extirpa-

tion, recurrence is not to be anticipated in as large a proportion of cases as is observed in growths situated elsewhere. For the same reasons recurrences following the class of cases just cited are more apt to be dyscrasial than regionary. Again, separating those of the lip, which are epitheliomatous in character, from those of the breast, which belong to the glandular variety, it is found that recurrences, both regionary and dyscrasial, are more frequent in the latter than in the former. It is likewise a well-known fact that locality has considerable influence in determining the question of recurrence. For instance, the disease, as it attacks the lips, cheeks, face and nose, is far less prone to lead to recurrence than in other situations, such as the tongue and larynx. It therefore may be said, in estimating the expectancy of life in a carcinomatous patient, that this will depend upon the malignancy of the disease, this being based upon the rapidity of its growth, if not operated upon, and the probability of its return, based upon its location and the stage of the disease reached before extirpation was advised or permitted. In regard to the latter it may be further stated that, while very early operation cannot positively insure against recurrence, on the one hand, on the other some cases have undoubtedly occurred in which operative interference has been postponed until after lymphatic glandular involvement had taken place, and yet no recurrence followed. Still, it is the experience of surgeons that early and radical extirpation of the primary focus holds out the most promising hope of cure. Not only this, but the dangers of the operation itself are very much lessened by adopting this course. In former times the growth was looked upon as the local expression of a general disease, and as a consequence the necessity for urging early removal not appreciated. At the present time, however, the diseased focus is looked upon as being locally restricted, and recurrences are not regarded as the result of a dyscrasia which existed from the beginning, but rather as evidence that the operation was undertaken too late, or was not sufficiently radical.

While every reasonable effort to effect a radical removal should be countenanced and encouraged, yet there will always remain a class

of cases the exigencies of which demand the application of palliative measures only. This is more particularly true of certain rapidly proliferating growths within the cavity of the uterus, upon the vaginal wall, etc. Here hæmorrhage and the constant presence of offensive discharge may temporarily, at least, be abolished by the use of the curette and thorough cauterization subsequently.

Experience teaches us that early enucleation by the knife in primary growths, and prompt and thorough removal of secondary deposits, and recurrences give the most satisfactory results. Although this is contrary to the general opinion held, yet the argument is altogether in favor of the attempt to rid the patient of the disease. In my own experience, nearly a year of life was gained, on an average, among those operated upon for carcinoma of the breast, as compared to those not operated upon.

A word as to methods of treatment of a non-operative character. Intra-parenchymatous injections of tincture of iodine, nitric acid, ozone water, and, more recently, of the solutions of the aniline coal-tar products, methyl-violet and carmine, etc. (Mosetig-Moorhof), have been tried. With the possible exception of the last named, there can nothing be said in favor of these procedures; the originator of this latter does not claim that a single case has been cured by it, and one observer (Le Dentu) declares that in a series of cases in which he tried it, in the majority the growth of the neoplasm was hastened.

The treatment of inoperable cases of carcinoma by means of inoculations of pure cultures of the streptococcus pyogenes of erysipelas has been recommended by P. Bruns. The method is not devoid of danger, and fatal results have been reported as being due to the inoculation, by Feichenfeld. The objection to the employment of such means consists in the very great undesirability of producing conditions in which the element of danger enters very largely, and which may pass completely beyond the control of the surgeon.

The destruction of the neoplasm by means of caustic paste has been attempted for many years past. These attempts have never gained the confidence of the profession, this being due in part, at

least, to the fact that the method has been to a great extent employed by irregular practitioners and ignorant quacks. The employment of the method by intelligent and conscientious members of our profession can only determine the precise value to be attached to the use of caustics in the treatment of carcinoma.

The use of internal medication in the treatment of carcinoma deserves a passing notice. If by this term, however, is meant such specific medication as will influence the course of the disease favorably, it can only be said that such has not as yet been discovered. The powdered oyster shells, cundurango, chloride of bromine, Chian turpentine and arsenic of modern times, have been found to be just about as efficacious as the roasted lizards and amulets of the ancients.

The remedy, above all others most useful internally, is that given solely and entirely for the relief of pain, namely, opium. When this has been said all has been said which can, in the present state of our knowledge, be deemed apropos of the internal use of medicines in the treatment of carcinoma.

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